SCREENING OF DEPRESSION IN PATIENTS WITH CARDIOVASCULAR DISEASE IN A TERTIARY CENTRE IN TRINIDAD AND TOBAGO: DEPRESS CVD TNT STUDY

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ABSTRACT

Objectives: This was an observational study aimed to screen patients with cardiovascular disease for depression in Trinidad and Tobago in a tertiary centre and to determine if there is a significant association between patients with symptoms of depression and other comorbidities.

Methods: Patients (N=1203) were randomly selected from the outpatient cardiology clinics at the Eric Williams Medical Sciences Complex. After fulfilling the inclusion criteria and informed consent were obtained, they were given the case report form which included the Patient Health Questionnaire 9. Results: The study had a 96% respondent rate whereby the average age was found to be 62 years old. 47.5% were male and 52.5% were female. 90.2% of the sample had cardiovascular disease. 25% of the sample had a PHQ score or greater than or equal to 10 with 19.3% having no symptoms of depression. Females were found to be more depressed than males (p < 0.001) and only ticagrelor use was found to be significantly associated with depression (p 0.001). Comorbidities associated with depression included hypertension, stroke, chronic obstructive pulmonary disease and chronic kidney disease excluding diabetes mellitus.

Conclusion: Approximately one in four patients with cardiovascular disease have significant symptoms of depression. Significant associations were found between depression and other illnesses. Thus, it is evident that screening for depression should be encouraged among patients with cardiovascular disease so that patients can be treated optimally and effectively to obtain the best outcomes. Further studies are needed to support these findings.

Keywords: cardiovascular disease; depression; comorbidities.

ACKNOWLEDGEMENTS

The willingness to participate in the study from the patients of the cardiovascular outpatient clinics was immensely appreciated. The research study was approved by the Research Ethics Committee of the University of the West Indies, St. Augustine and additionally, by the North Central Regional Health Authority. The assistance and approval from the Public Health Observatories at Eric Williams Medical Sciences Complex allowed the investigators of the study to use the facility as a research site which assisted in obtaining a large pool of patients with cardiac disease amongst Trinidad. The patients and the doctors of the cardiology outpatient clinics at Eric Williams Medical Sciences Complex were additionally of great assistance to conduct this study as these patients were all part of the clinic listings on each particular day. The staff of the cardiology outpatient clinics were very accommodating and provided a comfortable environment for the participants of the study.

No funding or sponsorship was obtained for this study and no conflict of interest was declared.

INTRODUCTION

Coronary artery disease, as well as depression, are both highly prevalent diseases. Both of them cause a significant decrease in quality of life for the patient and impose a significant economic burden on society(1). The evidence is growing that depression per se is an independent risk factor to suffer a cardiac event and thus if physicians become more aware of the prevalence of depression, this can impact on treating the condition and overall reduce the rate of morbidity/mortality in these patients.

Depression is highly prevalent in cardiac patients. Approximately 31-45% of patients with cardiac disease which include, coronary artery disease, suffer from clinically significant depression with 15-20% of patients with coronary artery disease meeting the criteria for major depressive disorder(2). Additionally, depression was found to be' more prevalent among females(3). Some cardiovascular diseases, such as atrial fibrillation, heart failure and patients who are awaiting implantation of implantable cardioverter-defibrillator devices have been noted to have increased risk for depression and major depressive disorder(2). It has also been observed that patients with cardiovascular disease have also been found to have other psychiatric illnesses such as generalized anxiety disorders, major depressive disorders and post-traumatic stress disorders(2).

Of significance, 25-45% of patients in Trinidad and Tobago with organic diseases have been noted to have features of depression(4). Suicides rates have been as high as 12.3/100 000 in Trinidad and Tobago(4). In 2008, 58% of males in Trinidad and Tobago died premature deaths as a result of cardiovascular disease while 69% of females died premature deaths as a result of cardiovascular disease which were between the ages of 30 years old to 69 years old(5). Therefore, we see that independently, the incidence of depression and cardiovascular disease in Trinidad and Tobago is considered to be

remarkable. It was additionally observed that 40% of hospitalized patients with existing cardiovascular disease had clinical depression in a public health institution in Trinidad in one study previously done(6). In this study, patients were screened for depression using the patient health questionnaire.

Comparatively, in another study, using the Centre for Epidemiologic Studies Depression scale done in Trinidad, it was found that 47% of patients with self-reported cardiovascular disease had depressive symptoms while 37% of patients with depressive symptoms have no self-reported cardiovascular disease(7).

One may question, what is the actual cause of depression; after much research, a myriad of hypotheses and theories have been postulated such as genetic and psychosocial stress related, stress hormone and cytokine-related, monoamine related, the neurotrophic hypothesis of depression, circadian rhythm related to altered glutamatergic and gabaergic neurotransmitter related(8). Thus, based on supporting and non supporting data for the above, depression is considered an etiologically heterogeneous disorder(8).

In comparison, the pathophysiology of cardiovascular disease ranging from acute coronary syndromes, heart failure to cardiac arrhythmia disorders, for the most is well understood. Data have suggested a causative relationship between depression and cardiovascular disease. One such culprit as a common finding to be the initiator of both diseases is inflammation(9). Inflammation has been shown to be abnormal with some consistency in mood disorders, however, cannot account for the entirety of the link between the two disease processes(9).

Depression is considered to be a risk factor for developing cardiovascular disease as it has biological effects, including abnormalities of endothelial function, atherosclerotic plaque integrity and changes in thrombosis or hemostasis as well as electrophysiological effects(10). The American Heart Association recommends that depression should be recognized as a risk factor for coronary heart disease just as hypertension, hyperlipidemia and diabetes mellitus(11). There is an 80% risk in developing worsening cardiovascular

disease and in addition to an increased mortality rate in adults with depression with or without previously existing cardiac disease (11). Based on a number of studies, there has not been any clear objective evidence to suggest a causative effect of depression on cardiovascular disease, as one is a mind related illness and the latter is a somatic disease, making it far more complex in reality to understand(12).

Depression has been shown to have a negative impact on patients with cardiovascular disease with respect to lifestyle, treatment and compliance(11). Thus, even though there is no objective evidence for a causative relationship between depression and cardiovascular disease, without a doubt, depression plays a major role in fitting the risk factor profile for cardiac disease. Additionally, depression is associated with a reduced quality of life and worsens the prognosis of cardiovascular disease(13).

This then leads to the next matter to discuss. How would treating depression impact on cardiovascular disease and mortality and vice versa? It is unknown whether successful treatment of depression impact on reducing cardiac morbidity and mortality based on some studies(14) (15). Additionally, antidepressants especially SSRI therapy and cognitive behavioural therapy have been found to be safe to use in patients with cardiovascular disease(14). Treating the symptoms of depression in the cardiac group of patients can aid in encouraging compliance with medications(1) and accurate and timely assessment of depression in patients with chronic heart disease has the potential to influence prognosis and reduce suffering in those who have been discharged after hospitalization for cardiac issues(16).

Hence, when depressive symptoms are treated successfully, there is a reduction of cardiac mortality and morbidity due to improvement in compliance with medication therapy and treatment strategies(15). From the Enhancing Recovery in Coronary Heart Disease Study (ENRICHD study), treating patients with depression with cognitive behavioural therapy reduced mortality and recurrent myocardial infarction, but there was no evidence to support a reduction in general cardiac morbidity and mortality outcomes(17).

In this study, the cohort was 2481 patients. With respect to the pharmacotherapy of depression, a potential side effect of tricyclic antidepressant therapy can cause lengthening of the cardiac myocyte action potential, less so for tricyclics and SSRI class of antidepressant medications. The potential risk of this can lead to precipitating cardiac arrhythmias(18) (19). However, in a 5 year follow up study, there was no increased risk for cardiac arrhythmias associated with antidepressant class; this risk was increased in the first 28 days when using tricyclic antidepressants while fluoxetine use did not reveal this finding and there was a significantly lower risk associated with its use for cardiac arrhythmias(20).

Due to SSRI medications being safer than other classes of antidepressants in patients with cardiac diseases, they are usually effective and the antidepressant of choice in a setting of cardiac disease(18). Particular precautions should be taken in treating patients with cardiac failure with antidepressants especially in those with prolonged myocyte action potentials(18). On the contrary, beta blockers particularly propranolol and atenolol along with calcium channel blockers can potentially cause depressive symptoms and are drugs used to treat cardiac disease(21).

It has been known that low socioeconomic status is a determinant for health and more specifically cardiac disease. Those with poor social support have an increased risk for cardiovascular disease(22). Similarly, low socioeconomic status has also been associated with a higher prevalence of depression(23). Using income and education level as a measure of the socioeconomic index, it was found that the index can be used to predict depressive symptoms(23). Thus, it can be seen that a lower socioeconomic status can imply a higher risk for cardiac disease and depression.

Age is noted to be an independent risk factor for the development of cardiovascular disease(24). Increasing age has generally been associated with a higher risk for developing cardiac disease possibly as there is an increased risk for traditional risk factors such as diabetes mellitus and hypertension with increasing age(25).

It has been hypothesised that a similar relationship exists for increasing age associated with depression, however, this has not yet been confirmed statistically(26). Thus, increasing age does play a role in the two diseases; but confounding variables such as socioeconomic status, in such populations, should be taken into consideration.

Interestingly, it has also been suggested that lower education levels are not associated with an increase in the incidence of cardiovascular disease in a study done among 20 543 Japanese women over a 12 year period(27). In another study done in a group of women, there was also an association between lower education levels being associated with a higher morbidity and mortality rate amongst females with cardiac disease(28). Some literature suggests that the link between low education levels and depression is not that clear as this relationship is deemed as inconclusive(29). Whilst, in other articles, reviewed it was suggested that lower levels of education increase the risk for depression and major depressive disorder(30). Therefore, there is some element with low education attainment increasing the risk of both depression and cardiac disease and this factor should not be ignored.

South Asian ethnicities have a higher risk of cardiac disease, specifically, ischemic heart disease whilst African Caribbeans have a lower risk of ischemic heart disease(31). However, black Americans have an increased risk of cardiovascular disease(32). Internationally, it has been noted that the prevalence of depression is more common amongst white Americans and Mexican Americans in the United States of America(33). In Trinidad, it was found that double the number of Indo-Trinidadians are depressed compared to Afro-Trinidadians(34). Ethnicities/racial groups do have a significant influence on the disease process involved in cardiac disease and depression and should always be taken into consideration.

Comorbidities most commonly associated in patients with depression include acute coronary syndrome, cancers and stroke(35). This may negatively impact on the disease processes and depression should be treated, as most times there is a deterioration in functionality, while these patients are safely monitored(35). The two most commonly reported medical illnesses in

association with depression are cardiovascular disease and diabetes mellitus(36). Of note, depression is not just associated with other physical medical comorbidities but also other mental illnesses such as anxiety disorders, alcoholism, obsessive compulsives disorders and personality disorders(37). In all, comorbidities other than cardiovascular disease should be noted as they can additionally be linked to depressive symptoms.

Approximately 31-45% of patients with coronary artery disease also had clinically significant depressive symptoms(2). About 36% of patients with heart failure had depressive symptoms while 30-40% undergoing coronary artery bypass graft surgery had depressive symptoms(2). Ischemic heart disease appears to be the most common type of cardiac disease associated with depression.

There are a number of investigational tools and screening questionnaires used to assess symptoms of depression such as the Beck's Depression Inventory, Patient Health Questionnaire- 2, Patient Health Questionnaire-9 and the Zung depression rating scale to name a few. The Patient Health Questionnaire – 9 has been shown to have reasonable sensitivity and specificity for patients with chronic heart disease(38) and hence is the investigational tool in this study. It is noted to be a quick screening test for depression. This questionnaire seems to assess any type of mood impairments rapidly and reliably, minimizing possible underestimates or misjudgments of the depressive symptomatology from both the patients and cardiac unit professionals. It is considered to be the gold-standard in the hospital setting(39).

It is recommended that physicians use tools such as the Patient Health Questionnaire-9 to screen cardiac patients for depression as there is a link between depression and cardiac disease and it is considered to be a bidirectional relationship(40). When compared to the Patient Health Questionnaire-2, the Patient Health Questionnaire-9 was found to have a higher sensitivity and specificity(41). It has been evaluated and shown that the Beck's Depression Inventory II and Patient Health Questionnaires are most useful in this setting of assessing patients with cardiac disease for

depression(39). In another study where the Patient Health Questionnaire-9 was administered as a self-assessment, it was found to have high sensitivity and moderate specificity(42). The Patient Health Questionnaire-9 has also proven to be useful in resource-poor settings(43).

Other advantages of the Patient Health Questionnaire-9 include that it is a quick assessment, it grades the severity of depression, can be obtained in different languages, the score is easy to calculate and additionally it can be used to reassess patients on antidepressant therapy as it grades depression(44). On the other hand, the downside of the Patient Health Questionnaire-9 is that it may lead to unnecessary diagnosis of depression and it does not include exclusion criteria for other mood disorders in which some patients can be misdiagnosed(44).

Based on the above, it can definitely be said that there is a link between depression and cardiac disease. But what is the importance of this link or relationship? The aim of establishing this relationship in Trinidad amongst a large patient population would allow physicians to treat patients optimally and be aware of depression being considered a risk factor for cardiac disease. It may additionally, help to increase screening for depression in the cardiology clinics as if depression is treated appropriately in this cohort of patients, the standard of care will without a doubt, improve as controlling and managing risk factor of a disease may assist in elimination or reduction of cardiovascular disease. This initiative may encourage patients to become more compliant with therapy and have a reduction in the morbidity and mortality rates associated with cardiac disease in Trinidad. It will also assist this group of patients to practise autonomy when it comes to their healthcare and has a positive impact on their functionality and lives overall.

Thus, it is important to determine the incidence of depression amongst the cardiac patients in Trinidad, to not just initiate treatment, but to further establish and raise awareness of this bidirectional link between depression and cardiac disease. In summary, depression is considered to be an independent risk factor for cardiac disease. In addition, other variables such as

socioeconomic status, ethnicity, educational level, medications and other comorbidities do have an impact on depression as well in this particular group of patients.

The Patient Health Questionnaire-9 is a good screening tool that can be used not just for detecting depression, but also for grading depression severity and aid with determining response to treatment. Hence, its use in this study. It is a quick assessment tool where its advantages outweigh its disadvantages and some studies have shown it to be an eye-opening self-assessment tool as well. Additionally, if patients are found to be depressed using this screening tool, they would be referred to a psychiatrist for further evaluation and treatment. This would encourage physicians to treat their patients as a whole being and not just focus on their cardiovascular health as there are many connections such as depression. It would also allow doctors to have a baseline screening score from the Patient Health Questionnaire-9 which is easy to redo and reassess patients at any point in time on treatment.

There are a number of studies in the pool of literature which show a relationship between depression and cardiovascular disease; however, this study aims to raise awareness and implement a change amongst the patients in Trinidad and Tobago with cardiac disease so that it would encourage and assist physicians to provide optimal health care for patients. It is also aimed to screen these patients for depression as in the cardiology clinics, depression is highly underdiagnosed and undertreated.

METHODS

The study design was a cross-sectional descriptive study performed from November 2018 to February 2019. It was performed at the Eric Williams Medical Sciences Complex, Champ Fleurs, Trinidad. Of note, this is one of the major public hospital institutions in Trinidad under the North Central Regional Health Authority whereby there is access to a 24-hour Accident and Emergency department where routine medical care is accessible. The population of Trinidad and Tobago is approximately 1.37 million people(45), in which the north-central distribution of the country seeks health care at this institution making it an excellent research site for this study.

The primary objectives of the study were to screen patients for depression in

The primary objectives of the study were to screen patients for depression in those with cardiovascular disease in Trinidad and Tobago and to determine the association between patients with depression and other comorbidities.

Patients for the study were recruited from the cardiology outpatient clinics at Eric Williams Medical Sciences Complex as this institution has a very strong cardiology background. Patients were targeted for participation in the study while waiting to see the attached physician to the cardiology clinic. Participants were attained at the Eric Williams Medical Sciences Complex during the days Monday to Friday where there were ongoing cardiology outpatient clinics. Once informed consent was obtained from these patients, a questionnaire was administered to these patients in which the primary investigator and/or co-investigator was/were present on site. The number of participants in this study was 1203 patients. There were no dropped subjects from the study nor were there any incomplete questionnaires by any participants. The sample size for this study was calculated to be 1159 patients. This was calculated using the MGH Biostatistics Calculator (46). The value obtained using this calculator was multiplied by 0.1, the attrition rate of the study and then subtracted from the original value obtained using the original value that was calculated using the MGH Biostatistics Calculator.

Based on a study done by Huffman, it was estimated that 40% of patients with cardiovascular disease also have depression(2). The Type I error rate 5% (α = 0.05) making the Type II error rate 95% (β = 0.95) with a statistical power of 90%. Assuming a 10% patient decline and attrition rate and a minimum detectable difference of 10%, the estimated sample size was calculated to be 1159 patients.

Data collection was performed by the researchers of the study along with eight specifically trained and oriented medical students. All data collectors in the study were supervised by primary investigator and co-investigator of the study so that in the event of any adverse events such as acute psychosis or any acute cardiology emergencies, patients could have been referred directly to the accident and emergency department at Eric Williams Medical Sciences Complex where routine medical care could have been executed. Of note, there were no adverse outcomes that occurred in the data collection process during this study.

Before ethical approval could be obtained, the co-investigator listed in this study had to complete a recommended and required ethics course by the University of the West Indies, St. Augustine. The ethics course was able to educate the researcher on ethical principles such as informed consent, privacy and confidentiality and conflicts of interest associated with research and was instituted by the Collaborative Institutional Training Initiative (CITI) associated with the University of Miami. It comprised 22 compulsory modules with 2 elective modules. Completion of this ethics course was confirmed with certification from the institution which was forwarded to the University of the West Indies, St. Augustine.

Ethical approval was obtained for this study to be performed from the ethics committee of the University of the West Indies, St. Augustine. Additionally, approval was obtained from the Head of Cardiovascular Department along with the Complex Administrator at Eric Williams Medical Sciences Complex. Approval was also granted from the Chief Executive Officer and from Public Health Observatories at Eric Williams Medical Sciences Complex in order to

use the complex as a research site to ensure that patients were safe and that no harm was done for the purpose of research. All of the prior mentioned approvals were forwarded to the cardiology outpatient clinic staff members.

Additionally, there was an attached consent form which was also approved by the ethical committee of the University of the West Indies, St. Augustine. This consent form clearly explained to the participants why the research was being conducted, the average duration of completing the questionnaire, the benefits and any potential risks associated with participation in the study along with the assurance that confidentiality will be maintained throughout the entire study and that the patient can stop or not complete the questionnaire at any point without any facing repercussions. This information was documented on the consent form and also explained by the researchers of the study to each potential participant. All additional questions from patients were answered truthfully regardless of if it would have affected the patient's decision to participate in the study.

Patients were asked to participate in the study as long as they were registered patients at Eric Williams Medical Sciences Complex in any of the cardiology outpatient clinics. This was confirmed by matching patients with their registration numbers on the cardiology outpatient clinic appointment listings. These lists are made prior to each cardiology clinic that is scheduled every week on Mondays, Tuesdays, Wednesdays, Thursdays and Fridays. The inclusion criteria for participation in the study included patients who were 18 years old and over along with registered patients of the cardiology outpatient clinics at Eric Williams Sciences Complex. The exclusion criteria for participants included patients less than 18 years old, those who did not give informed consent to participate in the study, patients who were not registered patients of the cardiology outpatient clinics at Eric Williams Medical Sciences Complex along with patients who were acutely unwell requiring hospital admission. No particular gender groups were excluded from this study. In addition, no ethnic and or racial groups were excluded from the study.

Patients who fit the inclusion criteria were approached and then given a written informed consent form which was approved by the Ethical Committee of the University of the West Indies, St Augustine, explaining the purpose of the study, the information collected from the participants of the study and what will be done with the recorded data as mentioned above. Commercial advertisements including the Internet and newspapers were not used to recruit patients in this study. Of note, no rewards or incentives were offered to encourage participation in the study by subjects nor were there any penalization for declining participation in the study. Specifically, patients were not offered any monetary payments to encourage their participation in the study. Patients were allowed to decide on their own, whether or not they wanted to participate in the study. Subjects were able to participate based on the fulfilling inclusion criteria and informed consent attained. Of significance, there was no sponsorship obtained to conduct this study.

Confidentiality of patients was kept and ensured as no patient names were recorded and all data recorded was de-identified. Patients were uniquely identified using their clinic registration numbers of the cardiology outpatient clinic. By using registration numbers to identify patients, this assisted in preventing duplicate collection and entry of data. Additionally, the database was only accessible to the primary investigator and the co-investigator of the study. The data was stored on a device which was password protected and again this password was only available to the primary investigator and co-investigator of the study. The database was encrypted to ensure the patient's recorded information was safe

In addition, there is an immense amount of literature on cardiovascular disease associated with depression. One of the hallmarks of this study would have been to choose the best screening tool for depression in this setting and the population of the cardiology outpatient clinics at Eric Williams Medical Sciences Complex. The depression screening tool used in the questionnaire of this study was the Patient Health Questionnaire-9. It was selected to be used in this setting in comparison to other depression screening tools as it is quick which would maintain patients' attention and prevent them from being too

preoccupied and missed seeing the physician in the cardiology outpatient clinic. Based on the literature, it is one of the better selections for a population to be screened where results are quick. This tool also allowed researchers to assess the category of depression into mild, moderate and severe. This allowed patients who were high risk to be easily identified in the event of any need for admission to the hospital facility.

The potential risks associated with asking questions listed in the Patient Health Questionnaire-9 were low. These potential risks included psychological trauma, feelings of depression and acute psychosis. Participants were monitored in the study during the questionnaire by the primary investigator and or of the study for any potential risks. If any risks were detected clinically, patients had the opportunity to be referred to the 24-hour accident and emergency department of the Eric Williams Medical Sciences Complex for further evaluation, admission and treatment. Fortunately, during this study, there were no occurrences of adverse events and no participants had to be referred to the accident and emergency department.

Of importance, no invasive data was collected from participants in this study. No blood samples were drawn and no drugs being tested were administered to any patients enrolled in the study. Additionally, any patients deemed as medical emergencies had the opportunity to be referred to the accident and emergency department of Eric Williams Medical Sciences Complex where the routine medical protocol was followed and appropriate referrals were made. Some examples of these emergencies included acute psychosis, acute coronary syndromes and acute heart failure.

The scores of the Patient Health questionnaire-9 were verbally communicated to the patients in confidentiality by the primary investigator and or co-investigator of the study along with the interpretation of the score and what it meant on the depression scale. Patients were given the opportunity to decide if they wanted these results communicated to the physician seeing them in the cardiology outpatient clinic and if so; the results were given to their respective

physicians who would have decided on appropriate referrals and routine medical care. This would include appropriate referrals to psychiatry.

The Social Sciences 24 (SPSS, Chicago, Illinois USA) was the software used for the entry of data and its analysis. Descriptive analyses were performed which were unadjusted. Statistical significance was accepted as p < 0.05.

RESULTS

Out of 1253 patients being approached to participate in the study, 1203 gave informed consent to participate in the study, giving an overall response rate of 96%. Based on Table 1, the average age of the study population was found to be approximately 62 years old with the distribution of the study population being 47.5% male and 52.5% female. There were no other genders groups such as lesbian, bisexual and gay in the study population. Based on the educational background of the study population, the majority of patients has a background of up to primary school education of 49.5% while just 6.6% of the population has a background of no education. The income levels of these patients ranged from 28.2% of patients having no income at all, with 52.5% of patients being pensioners who received a pension income. Of note, only 3.1% of the population has earnings of more than \$10 000.00. The majority of patients in the study was of Indo-Caribbean descent making up 57.4% of the participants. Afro-Caribbean ethnicities made up approximately 31.5% of the participant group.

Demographics (N=1203)	Value
*Age (years)	62.5 ± 13.1
+Gender	
Male	571 (47.5%)
Female	632 (52.5%)
+Education	
None	79 (6.6%)
Primary	595 (49.5%)
Secondary	400 (33.3%)
Tertiary	129 (10.7%)
+Salary	
None	339 (28.2%)
Pension	631 (52.5%)
5000-10 000	196 (16.3%)
>10 000	37 (3.1%)
+Ethnicity	
Indo-Caribbean	690 (57.4%)
Afro-Caribbean	379 (1.5%)
Mixed/Other	134 (1.1%)

^{*}Mean ± Standard deviation

Table 1: Demographics of Sample

⁺Frequency (Percentages)

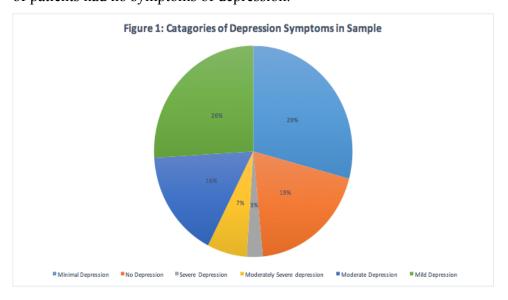
Table 2 illustrates the distribution of diseases of the study population out of 1203 patients. 90.2% of these patients had coronary artery disease/ cardiovascular disease. 9.8% of these patients were registered patients of the cardiology outpatient clinics who were referred for suspected cardiac disease and had pending cardiac investigations such as coronary angiograms and transthoracic echocardiograms. Additionally, many of these patients had lifestyle diseases where 47.9% of patients were diabetic and 71.5% of patients were hypertensive. Approximately 51.0% of these patients also had hyperlipidemia. Only a small percentage of the sample population had COPD which was 5.7% of the sample of participants.

Disease (N=1203)	+Value
Coronary artery disease/ cardiovascular disease	1085 (90.2%)
DM	576 (47.95%)
HTN	860 (71.5%)
Hyperlipidemia	614 (51.0%)
COPD	69 (5.7%)
Chronic kidney disease	101 (8.4%)
Stroke	139 (11.6%)
Peripheral vascular disease	115 (9.6%)

⁺Frequency (percentages)

Table 2: Disease Status of Sample

With respect to the patients who had symptoms of depression based on the Patient Health Questionnaire-9 scores, a PHQ score of 10 or more was used as a cut off to represent the percentage of patients with significant symptoms of depression. The PHQ more than or equal to 10 has been noted to have a specificity and sensitivity of 88% for major depression(47) and hence, why it was used as the score for significant depressive symptoms. Figure 1 depicts the distribution of the sample population with respect to PHQ scores. A total of approximately 25% of patients had a PHQ greater than or equal to 10 representing severe depressive symptoms. Only a small percentage of 19.3% of patients had no symptoms of depression.



826 patients were on aspirin therapy. This accounted for 68.7% of the sample population while 31.8% of patients were on clopidogrel. Additionally, 53.5% of patients were on a statin. 17% of patients were on calcium channel blockers as compared to 44.7% of patients were on beta-blocker therapy. Only approximately 2.2% of patients were on ticagrelor therapy. 9.3% of patients were on warfarin and 1.2% of patients were on Factor Xa inhibitor drugs. The distribution of medication use can be seen in Table 3.

From Table 4, the female population was found to have more depressive symptoms than the male population with a p-value of <0.001. Other statistically significant findings were that patients with no education or secondary level education were found to be depressed and had PHQ scores of more than or equal to 10. Very low-income brackets and very high-income bracket patients were also found to be more depressed in this sample of patients using Fisher's Exact test. Chi-squared testing revealed no associations between depression and ethnicity in this population of patients.

With respect to medication use, the only significant association between depression and medication use was found with ticagrelor with a p-value of 0.001. Out of 304 patients with PHQ greater than or equal to 10, 4.9% were on ticagrelor. There were no statistically significant associations found between depression and the use of beta blockers, calcium channel blockers, analgesic use, ACE inhibitors, ARBs and statins. This can be seen clearly in Table 5.

The number of diseases was positively correlated with having major depression with an odds ratio of 1.248 (95% Confidence Interval: 1.125-1.384) Additionally, the number of drugs was positively correlated with having major depression with an odds ratio of 1.062 (95% Confidence Interval: 1.005-1.123).

When adjusted for age, gender, ethnicity, salary and education, there were a number of diseases associated with depression in this study. Hypertension, COPD, chronic kidney disease and stroke were all significantly associated with depression. When adjusted, the odds ratio for hyperlipidemia associated with depression was 1.263 (95% CI 0.965-1.653), making it not statistically significant.

In summary, approximately 25% of the sample population had significant symptoms of depression in which their PHQ score was greater than or equal to 10. Significant association were found with comorbidities such as hypertension, COPD, Chronic kidney disease and stroke. Associations were also found between depression and the use of ticagrelor. Additionally, the

female gender had a tendency to be more depressed, along with low salary brackets of income and pensioners being more depressed.

Drug (N=1203)	+Value
Aspirin	826 (68.7%)
Clopidogrel	382 (31.8%)
ACE inhibitors	505 (42.0%)
ARB	150 (12.5%)
Beta Blockers	538 (44.7%)
Statin	644 (53.5%)
Ivabradine	88 (7.3%)
Trimetazidine	313 (26.0%)
Nitrates	282 (23.4%)
Spironolactone	61 (5.1%)
Calcium channel blockers	204 (17.0%)
Loop diuretics	211 (17.5%)
Vitamin K antagonists	112 (9.3%)
Factor Xa inhibitors	14 (1.2%)
Analgesics	23 (1.9%)
Ticagrelor	27 (2.2%)

Table 3: Drug Use in Sample

⁺Frequency (percentages)

Demographic	PHQ < 10 (n=899)	PHQ ≥ 10 (n=304)	p value
di A	(0.55 + 10.1	60.00 . 12.1	0.050
*Age (years)	62.57 ± 13.1	60.88 ± 13.1	0.052
mean ± SD			
+Gender			
Male	463 (51.5%)	108 (35.5%)	
Female	436 (48.5%)	196 (64.5%)	< 0.001
+Education			
None	46 (5.1%)	33 (10.9%)	0.001
Primary	432 (48.1%)	163 (53.6%)	0.094
Secondary	317 (35.3%)	83 (27.3%)	0.011
Tertiary	104 (11.6%)	25 (8.2%)	0.109
+Salary			
None	221 (24.6%)	118 (38.8%)	< 0.001
Pensional	490 (54.5%)	141 (46.4%)	0.017
5000 – 10000	154 (17.1%)	42 (13.8%)	0.208
>10 000	34 (3.8%)	3 (1.0%)	0.012

Demographic	PHQ < 10 (n=899)	PHQ ≥ 10 (n=304)	p value
~Ethnicity			
Indo-Caribbean	510 (56.7%)	180 (59.2%)	
Afro-Caribbean	292 (32.5%)	87 (28.6%)	0.426
Mixed/Other	97 (10.8%)	37 (12.2%)	

^{*}Independent Sample t test

Table 4: Association between Demographics and Major Depression $(PHQ \geq 10) \label{eq:photoconstraint}$

⁺Fisher's Exact test

[~]Chi Square test

Drug	*PHQ<10 (n=899)	*PHQ ≥ 10 (n=304)	p value
Aspirin	606 (67.4%)	220 (72.4%)	0.116
Clopidogrel	291 (32.4%)	91 (29.9%)	0.476
ACE inhibitor	363 (40.4%)	142 (46.7%)	0.060
ARB	113 (12.6%)	37 (12.2%)	0.920
Beta blocker	399 (44.4%)	139 (45.7%)	0.689
Statin	473 (52.6%)	171 (56.2%)	0.287
Ivabradine	71 (7.9%)	17 (5.6%)	0.204
Trimetazidine	222 (24.7%)	91 (29.9%)	0.082
Nitrates	202 (22.5%)	80 (26.3%)	0.183

Drug	*PHQ<10 (n=899)	*PHQ ≥ 10 (n=304)	p value
Spironolactone	41 (4.6%)	20 (6.6%)	0.174
Calcium channel blocker	149 (16.6%)	55 (18.1%)	0.537
Loop diuretic	151 (16.8%)	60 (19.7%)	0.257
Vitamin K antagonists	81 (9.0%)	31 (10.2%)	0.568
Factor Xa inhibitor	11 (1.2%)	3 (1.0%)	>0.99
Analgesics	14 (1.6%)	9 (3.0%)	0.145
Ticagrelor	12 (1.3%)	15 (4.9%)	0.001

^{*}Frequency (percentages)

Table 5: Association between Medication use and Major Depression $(PHQ \geq 10) \label{eq:photoconstraint}$

Disease (Comorbidity)	Unadjusted Odds Ratio (95% CI)	*Adjusted Odds Ratio (95% CI)
HTN	1.821 (1.330-2.492)	1.988 (1.414-2.797)
Hyperlipidemia	1.347 (1.037- 1.750)	1.263 (0.965-1.653)
COPD	1.741 (1.046-2.897)	1.703 (1.009-2.876)
Chronic Kidney disease	1.896 (1.239-2.901)	1.872 (1.207-2.902)
Stroke	1.665 (1.142-2.427)	1.847 (1.251-2.728)

^{*}Adjusted for Age, Gender, Salary and Education

Table 6: Association between Diseases (Comorbidities) and Major Depression (PHQ $\geq 10)$

DISCUSSION

In this study, it was found that the mean of ages of the sample population was 62 years old in which the female patients were more likely to have depressive symptoms as compared to the males. This was not surprising as it has been found that depression is 1.7-fold greater incidence in women(48). This gender disparity has well been documented in the literature that the female gender is associated with a higher prevalence of depression (49). In another study supporting this finding, it was found that women are twice as likely to develop depression in their lifetime than men(49). Some postulated causes for this gender gap for depression emerge from biological sex differences and have less to do with other issues such as cultural differences, education and diet(48). In this study, 64.5% of females had depression symptoms determined by a PHQ score or greater than or equal to 10. The female and male distribution of the sample population in this study was approximately evenly distributed where about 52.5% were females. Additionally, another article suggested that women tend to have internalizing features of depression whereas men external features of depression(48).

Out of 1203 patients, more than 50% of the population had only up to primary level education. 10.9% of the population had no formal education was found to have significant symptoms of depression. Lower levels of educational attainment are associated with a higher rate of depression in the western world(50). From this evaluation, the association was not due to genetic effects but more environmental factors such as socioeconomic factors(50). The HUNT study found that there was a protective effect of higher levels of educational attainment associated with a lower risk for depression and anxiety; seeming to have a cumulative effect throughout life(29). Some proposed hypotheses for this protective effect include higher education level attainment aid in more satisfactory occupations with higher salaries, healthier lifestyle practices and better development of self-efficacy resulting in enhanced coping mechanisms with stressors associated with life(51). In China, it was found that lower levels of education were associated with a lower socioeconomic status which led to an increased likelihood for the development of major depressive

disorder in a female population that was studied(52). Consistent with the findings of this study, there was a positive correlation between lower levels of education and mental health in general in which the relationships were strongly related to employment and being in a relationship(53). Therefore, it can be seen that the relationship between low education levels and depression has been established throughout the western and eastern continents.

Patients that were found to have significant symptoms of depression (PHQ greater than or equal to 10) were found to have no salary earnings, pensionable earnings or those in the greater than \$10 000.00 salary bracket. In one meta-analysis done, it has been shown that depression is more prevalent in populations where there is a greater degree of income inequality(54). Another study also supported this finding was assessed using the European Social Survey 2006/2007 in which it was found that income inequality was associated with higher rates of depression (55). In assessing depression using the General Health Questionnaire, it was similarly found that 20-30% of people with depression were in the lowest income or wealth categories as compared to 10-15% were in the higher income brackets(56). Hence, demonstrating depression in the lowest and highest income brackets as found in this study. Family or household income seems to have some protective effect against depression as proposed in another study(57). Hypothesized theories to support these finding include two main theories of social causation and social selection(58). Depression may cause stress, reduced coping mechanisms and adversity which may be the aetiology of low-income settings and increased risk for the development of mental illness as proposed by the social causation theory (58). The social selection hypothesis that those with mental illness are more likely to have a reduction in socioeconomic status as a result of possible genetic factors, increased incidence of hospitalizations and increased rates of unemployment (58). On the contrary, it was also found that depression was more prevalent amongst those with higher income earnings compared to those with lower incomes in a meta-analysis and systematic review which included 26 studies(54). Those earning more than \$10 000.00 was found to have more significant symptoms of depression which was a statistically significant finding in this study.

There were no significant associations between any particular ethnic group and depression found in this study. In comparison. In another study which compared Whites, Hispanics and African Americans, it was found that depression was more prevalent among the minority groups (Hispanics and African American)(59). Possible explanations for these findings were that the minority groups were more likely to be female, lived alone, had one living parent and had more chronic diseases(59). The ethnic distribution of the patient population in this study was quite different. Likewise, there were higher rates of depression amongst African Americans and Mexicans with significant lower depression care use(60). Physical health among ethnic groups was another variable which impacted upon the rates of depression amongst different ethnic groups as it was found in England that South Asians were more depressed than Whites as a result of poorer physical health status(61). Of significance, it has been reported that foreign-born ethnicities have lower rates of depression when compared to non-foreign-born ethnicities in the United States of America(62). In another local study assessing hospitalized patients with cardiac disease for depression, no particular ethnic group was significantly more depressed as depicted in this study(6). Of note, there is a paucity of local data comparing Caribbean ethnicities and their association with the prevalence of depression.

90% of 1203 respondents were reported as having coronary artery disease/cardiovascular disease in the sample population. However, the remaining 10% of patients were still registered patients of the cardiology outpatient clinics at Eric Williams Medical Sciences complex with no confirmed cardiac diagnosis at this point of evaluation. This could occur as a result that there was no confirmed or objective evidence thus far, to confirm the presence of cardiac disease in these particular patients. For instance, some of these patients would have cardiac type symptoms and referred to a specialist cardiology clinic to be investigated for a disease process and thus, would be awaiting their investigations and results. Additionally, as it was an outpatient setting some of the results of investigations such as coronary angiograms, transthoracic echocardiography reports, physiological exercise stress test reports would still

be pending in which patients would routinely be seen while awaiting these investigations or results by their physicians to ensure no change or worsening in their symptomatology and to ensure no new symptoms arising for further evaluation and investigation. They were still included in the sample as they are registered patients of the cardiology clinics and they would have had symptoms to represent cardiac disease clinically at some point in their presentation.

Depression symptoms were prevalent in other disease conditions in this study. These included hypertension, chronic obstructive lung disease, chronic kidney disease and stroke after being adjusted for age, gender, salary and education levels. After the odds ratio was adjusted for age, gender, salary and education, hyperlipidemia was not significantly associated with depression. It was found that both diseases, depression and hypertension can impact on each other (63). Hence, patients who were depressed were found to have poorly controlled hypertension while patients with hypertension were found to have depression(63). The prevalence of depression in patients with hypertension was found to be 26.8%(64). Similarly, depression is common in patients with COPD. The prevalence of depression in COPD has been found to be approximately 40% which is much higher than those with hypertension(65). The relationship between COPD and depression also seems to be bidirectional and nicotine dependence associated with COPD seems to have a major impact on this occurrence(66). Likewise, there is a relationship between patients who suffered a stroke and depression. Depression was found to be 1.77 times more common in those patients with a previous stroke and linked to social distress after suffering a stroke(67). Patients with chronic kidney disease have also been found to have varying levels of depression(68). There have been studies which reported that patients with chronic kidney disease who have depression are undertreated(69).

Out of all the medication associations with respect to depression, the only ticagrelor had a statistically significant relationship with significant symptoms of depression. The drug ticagrelor is an antiplatelet, a direct-acting inhibitor of adenosine diphosphate receptor P2Y12(70). Conduction abnormalities have

been reported after an acute coronary event with the use of ticagrelor in a case reported in 2017(71) which been well documented in the literature. In the PLATO trial, out of 9235 patients, approximately 1.1% of patients experienced depression with ticagrelor(70). When compared to clopidogrel, the rate of depression was quite similar(70). Thus far, there have not been any major findings of depression associated with the use of ticagrelor as found in this study. 4.9% of patients had a PHQ of more than or equal to ten, who were taking ticagrelor. This finding may have been related to depression being associated with the disease that ticagrelor was being used to treat, coronary artery disease.

The categories of depression were divided into no depression, minimal depression, mild depression, moderate depression, moderately severe depression and severe depression based on the Patient Health Questionnaire-9 score. Patients with significant symptoms of depression were defined as a patient who had a PHQ-9 score of greater than or equal to ten. This cut off was used as it has been documented in the literature to have a sensitivity and specificity of 88% for detecting major depressive disorder(47). The PHQ-9 scores greater than or equal to ten would include the categories of moderate depression, moderately severe depression and severe depression. In this study, it was found that approximately 25% out of 1203 patients had significant symptoms of depression while only 19.3% of this population had no symptoms of depression. Approximately, 31-45% of patients with cardiac disease have been reported to be depressive symptoms(2). It can be clearly demonstrated that depression is without a doubt, underdiagnosed in the outpatient cardiology clinics at the Eric Williams Medical Sciences Complex. It should be noted that in this setting, the Patient Health Questionnaire - 9 was not used as a diagnostic tool but as a screening tool for depression as it has been well documented in the literature and has been shown to work very well for screening a population for depression(72). Additionally, it has demonstrated great use in determining the severity of depression(47). The phrase "depression" in this study was used to represent the risk for major depression or likelihood for meeting the criteria for the diagnosis of depression.

Of importance, out of 1203 respondents, no patients were previously diagnosed or gave a medical history of a formal diagnosis of depression even though approximately 25% of this population had significant symptoms of depression. Two patients were on fluoxetine therapy and alprazolam therapy for generalized anxiety disorder. In a population with cardiac type diseases, the prevalence of depression is three-fold higher than that of the general population and thus, has been well documented to be underdiagnosed in these patients(11), even though it has been reported as a risk factor for developing cardiac disease(11). Those who have depression with cardiac disease have a worse outcome than those who are not depressed (18). This finding may be supported as patients who are depressed are likely to be non-compliant with therapy for their cardiac condition(18). Thus, it is extremely important to screen this population of patients to reduce the rates of morbidity and mortality. It is recommended that patients with cardiac disease should be screened for depression so that the condition is not underrecognized and undertreated in an effort to improve the overall outcome of such patients. However, there are no studies which have shown that community-based screening for depression improves cardiovascular outcomes(73).

As previously mentioned, ticagrelor was the only drug from the study which was linked to patients demonstrating significant depressive symptoms. It is important to note that a pertinent negative finding from the study was that patients on beta-blocker therapy did not exhibit any significant symptoms of depression and this finding is supported in the literature. It was found that there was an only small risk of fatigue and sexual dysfunction associated with beta blockers but there was no increased risk for depression in using these drugs(74). Calcium channel blockers are common drugs using in the treatment of hypertension, a risk factor for cardiac disease and also depression.

Interestingly, there is some degree of controversy with respect to if calcium channel blocker therapy is linked to depression and increased suicidal rates. In an observational Swedish study, there was a significant correlation between the use of calcium channel blockers and increase the chance of suicide after being adjusted for age and sex(75). In this study, that correlation was not found between the use of calcium channel blockers and depression. Another

class of drug used in the treatment of coronary artery disease includes statins. In this study, there was no correlation between statin therapy and depression. However, in a Swedish cohort, it was found that statins, specifically simvastatin, may have some protective effect against depression, especially in patients over the age of 40 years old(76).

Unexpectedly, there was no association found between patients with diabetes mellitus and significant symptoms of depression even though some literature has supported this association. In another local study done in 2013, it was found that depression was significant among patients with diabetes mellitus, hypertension and those with heart disease(77). This association linking depression and diabetes mellitus was also found when studied in patients from Malaysia, where patients were found to be depressed likey as a result of diabetic complications (78). In the Madrid Diabetes Study, patients with type 2 diabetes were also found to have depression most likely as a result of their health status, mental status, diabetic complications and gender (79). One studied aetiology for this association of depression and diabetes mellitus may be linked to the use of insulin therapy as it was found that patients on insulin therapy had a higher risk of depressive symptoms (80). The importance of these associations between depression are other comorbidities lie in the fact that poorly controlled depression, poorly controlled diabetes mellitus and other poorly controlled diseases are linked to worse outcomes and result in an overall greater health care cost(81). Thus, the importance to observe these associations and aim to treat these diseases and not fail to notice symptoms of depression among this group of patients and it does have an impact on morbidity and mortality rates.

One assessment done using the Patient Health Questionnaire - 9 was functionality status. It is imperative to include this aspect of the assessment as it was found that the severity of depression increased, there was a decline in the functional status of individuals(47). The severity of depression is additionally essential to determine as individuals with more severe depression do worse(82). In another study which evaluated patients who were depressed, it as found that they had the tendency to an increased rate of poorer self-

reported role functionality(83). Self-reported low functional status could have been as a result of their emotional or physical conditions(83). Thus, it can be seen that an individual's functional status may be considered subjective if patients are self-reporting and run the risk of being over-reported. However, it is an important aspect in determining the severity of depression which can impact on the overall well being of a patient.

The Patient Health Questionnaire - 9 was chosen as to research tool in this study as it has been found to be a good screening tool for depression. It has been found to have a high sensitivity and negative predictive value, however, its sensitivity and a positive predictive value were low making it an excellent choice to screen patients for depression but not used to make a diagnosis(84). In our setting, it was applicable as the patients were willing to participate as the questionnaire only comprised a small number of questions. This made it easy to understand and not very time consuming, hence such a high respondent rate for the study. In addition, the Patient Health Questionnaire 9 has been proven to be useful across different cultural groups when used with different ethnic groups which included African-Americans, Chinese-Americans, Latinos and Whites(85) making it very useful in our setting which includes a variety of ethnic groups. One disadvantage of the Patient Health Questionnaire 9 is that it is not a diagnostic tool and thus, if patients score more than or equal to 10, they need further evaluation for the diagnosis of depression and using this questionnaire does not give a final diagnosis of depression(84). When the Patient Health Questionnaire 9 was compared to the Beck Depression Inventory II, both were found to have adequate reliability, convergent/discriminant validity and similar responsiveness to change(86). There were differences in the categorization of the severity of depression between the two(86). The Patient Health Questionnaire 9 was chosen to be used in this study as it was shorter and would not prevent or delay patients' clinic visits in the outpatient cardiology clinics.

The Patient Health Questionnaire 9 was used in one study in specialized outpatient clinics in Japan to screen diabetic patients for depression, in which this screening tool was found to be useful and effective (87). It has also been

found that the Patient Health Questionnaire 9 is an excellent screening tool in the primary care setting too(84). Additionally, this screening tool was also used to screen in patients with cardiac disease in Trinidad and Tobago. Hence, it has been seen throughout the literature that the Patient Health Questionnaire is useful and effective both in an inpatient and outpatient setting.

Of importance, in this study, patients who were found to have a PHQ score of greater than or equal to 10 were advised to seek further evaluation from a psychiatrist so that they can be formally assessed and diagnosed accurately. Once patients gave informed consent, these results were communicated to the physician who was attending to them in the cardiology outpatient clinic at Eric Williams Medical Sciences Complex, whereby routine medical care would be followed through and these patients would be given the appropriate referrals. It was reiterated to patients, that this questionnaire was a screening test and not a diagnostic test by any means. In the study, no respondents required admission to the emergency department at the Eric Williams Medical Sciences Complex.

It was also found that there were positive correlations between the number of diseases and depression along with the number of medications a patient was taking and depression. This would be supported as different comorbidities as previously mentioned are associated with a higher risk of depression and thus these correlations were not surprising.

In summary, it is evident that significant symptoms of depression were found in approximately 25% of patients with cardiac disease, which means one out of every four patients had depressive symptoms. Thus, closer attention is needed when it comes to screen such patient populations to assist in reducing the rates of morbidity and mortality and assist in compliance with medical therapies recommended. Additionally, further studies would be needed to evaluate if ticagrelor is independently associated with a higher risk of depression as found in this study. It should be noted that the Patient Health Questionnaire 9 is an excellent screening tool for depression and should not be used as a diagnostic tool by any means. Screening of depression should be

encouraged so that patients are effectively treated and patients who have depression are no longer underdiagnosed.

Strengths and Limitations

One of the major strengths if the study would be the number of participants of this study which was 1203 patients. This would have assisted to generalize the data that was analyzed across Trinidad and Tobago and give an idea of the incidence of depression amongst patients with cardiovascular disease across the country and have a greater impact on implementing therapy and making a change. Another strength worth mentioning in this study was the research site chosen, Eric Williams Medical Sciences Complex, as this is the only public health care tertiary institution that has a device cardiology outpatient clinic for cardiac patients with pacemakers, implantable cardioverter devices and chronic resynchronization therapy devices. Additionally, it is the only public health care institution which offers images services of CT coronary angiograms and cardiac MRIs along with invasive interventional cardiology procedures such as invasive coronary angiograms, percutaneous coronary intervention and coronary artery bypass graft surgery. Hence, this institution would have patients from the entire country and not just the north-central jurisdiction; including patients from San-Fernando, Port-of-Spain and Sangre Grande. This makes the data more plausible as it gives an overview of depression in cardiac patients with respect to most geographical locations of Trinidad and Tobago.

The Patient Health Questionnaire-9 is a short and easy questionnaire which is easy to understand between all levels of education. Patients were more willing to participate as the questionnaires took an average time of 5 minutes for completion and it did not get in the way of their appointments to see the physician in the cardiology outpatient clinic. Any terminology on the questionnaire which was not understood was verbally explained that the person administering the questionnaires. It was also a good screening tool for depression as the results were easy to interpret and communicate to the doctors of the cardiology outpatient clinic as long as patients gave their

consent for this to be done. This made it easy for a routine medical practice to be implemented on site.

There were some limitations of this study, one of which was the variability of patient responses with respect to questions being asked as this may have been inconsistent based on the patients' current mood, location, time and health status. As the study is a cross-sectional study, it only represents the participants' current feelings at one particular instance which is variable and likely to change.

Another possible limitation of the study included the patients' truthfulness with respect to their responses in the questions asked. Some responses may have intentionally not been the truth to prevent doctors' concern for mental health rather than cardiovascular health or that patients may have been embarrassed to state how they really feel.

As a result of needing the participants' consent to communicate the results of the Patient Health Questionnaire-9 with the doctors in the clinic, some patients with major depression based on the responses, may not have been able to have appropriate psychological and psychiatry intervention if consent was not obtained. This would have prevented routine medical care to be implemented.

Additionally, 9.8% of the respondent group did not have any confirmed diagnosis of cardiovascular disease as they were referred for the suspected diagnosis of cardiac disease but their investigations to confirm and provide objective evidence of cardiac disease were still pending.

One last limitation of the study to be mentioned is that the research site of this study was only 1 out of 5 public health tertiary institutions and may not have provided an accurate representation of depression amongst patients with cardiac disease in Trinidad and Tobago. Thus, more studies similar to this one would need to be carried out to assess patients of the other public institutions.

CONCLUSION

There is clear evidence to support the association of cardiovascular disease and significant symptoms of depression in Trinidad and Tobago. This finding is alarming and states in itself that depression is a condition which is tremendously undertreated in our setting. 1 in every 4 patient was found to have significant symptoms of depression in the sample population. Other factors may additionally influence the presence and severity of depression such as gender, lower levels of education and low socioeconomic factors, in particular, lower levels of income, which in all are all a multi-directional relationship.

Data obtained from this study can assist in instituting policies in the cardiology outpatient clinics at Eric Williams Medical Sciences Complex for the screening of depression amongst this particular group of patients and possible aid in the start of implementing treatment. It may even contribute to lowering the morbidity and mortality rates secondary to cardiac disease as a result of increased adherence and compliance to treatment plans.

Further studies are required at other public health tertiary institutions in Trinidad and Tobago to validate the findings of this study and assist to implement change to no longer understate depression associated with cardiovascular disease at a national level.

REFERENCES

- 1. Zellweger MJ, Osterwalder RH, Langewitz W, Pfisterer ME. Coronary artery disease and depression. Eur Heart J. 2004 Jan 1;25(1):3–9.
- 2. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and diagnosis. Cardiovasc Psychiatry Neurol. 2013 Apr 7;2013:695925.
- 3. Safaie N, Jodati AR, Raoofi M, Khalili M. Depression in coronary artery disease. J Cardiovasc Thorac Res. 2012 Sep 23;4(3):77–9.
- 4. Abel WD. The Epidemiology of Mental Health Issues in the Caribbean.

 Available from:

 https://www.paho.org/disasters/index.php?option=com_docman&view=downl
 oad&category_slug=books&alias=1973-mental-health-and-psychosocialsupport-in-disaster-situations-in-the-caribbean-chapter5&Itemid=1179&lang=en
- CVD-TRINIDAD-TOBAGO-PROFILE-2014.pdf. Available from: https://www.paho.org/hq/dmdocuments/2014/CVD-TRINIDAD-TOBAGO-PROFILE-2014.pdf
- 6. Bahall M. Prevalence and associations of depression among patients with cardiac diseases in a public health institute in Trinidad and Tobago. BMC Psychiatry. 2019 Jan 7;19(1):4.
- 7. Changoor TMR, Hutchinson G. The prevalence of depressive symptoms in a Trinidadian cardiac population. West Indian Med J. 2013 Sep;62(7):620–7.
- 8. Hasler G. Pathophysiology of depression: do we have any solid evidence of interest to clinicians? World Psychiatry. 2010 Oct;9(3):155–61.
- Fiedorowicz JG. Depression and cardiovascular disease: an update on how course of illness may influence risk. Curr Psychiatry Rep. 2014 Oct;16(10):492.

- Januzzi JL, Stern TA, Pasternak RC, DeSanctis RW. The Influence of Anxiety and Depression on Outcomes of Patients With Coronary Artery Disease. Arch Intern Med. 2000 Jul 10;160(13):1913–21.
- Chaddha A, Robinson EA, Kline-Rogers E, Alexandris-Souphis T, Rubenfire M. Mental Health and Cardiovascular Disease. Am J Med. 2016 Nov;129(11):1145–8.
- 12. Roest AM, de Jonge P. The heart of the matter: in search of causal effects of depression on somatic diseases. BMC Med. 2018 Aug 23;16(1):147.
- Kronish IM, Krupka DJ, Davidson KW. How Should We Treat Depression in Patients with Cardiovascular Disease? Dialog Cardiovasc Med. 2012;17(2):126–33.
- 14. Mavrides N, Nemeroff C. Treatment of depression in cardiovascular disease.

 Depress Anxiety. 2013 Apr;30(4):328–41.
- 15. Whooley MA. Depression and cardiovascular disease: healing the brokenhearted. JAMA. 2006 Jun 28;295(24):2874–81.
- 16. Kiropoulos LA, Meredith I, Tonkin A, Clarke D, Antonis P, Plunkett J. Psychometric properties of the cardiac depression scale in patients with coronary heart disease. BMC Psychiatry. 2012 Dec 3;12:216.
- 17. Vieweg WVR, Julius DA, Fernandez A, Wulsin LR, Mohanty PK, Beatty-Brooks M, et al. Treatment of Depression in Patients with Coronary Heart Disease. Am J Med. 2006;119(7):567–73.
- 18. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: a clinical review. Eur Heart J. 2014 Jun 1;35(21):1365–72.
- 19. Spindelegger CJ, Papageorgiou K, Grohmann R, Engel R, Greil W, Konstantinidis A, et al. Cardiovascular adverse reactions during antidepressant treatment: a drug surveillance report of German-speaking countries between

- 1993 and 2010. Int J Neuropsychopharmacol [Internet]. 2014 Oct 31;18(4). Available from: http://dx.doi.org/10.1093/ijnp/pyu080
- 20. Coupland C, Hill T, Morriss R, Moore M, Arthur A, Hippisley-Cox J. Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64: cohort study using primary care database. BMJ. 2016 Mar 22;352:i1350.
- 21. Rogers D, Pies R. General medical with depression drugs associated. Psychiatry . 2008 Dec;5(12):28–41.
- 22. Kumar S. Cardiovascular Disease and Its Determinants: Public Health Issue. Journal of Clinical Medicine and Therapeutics [Internet]. 2017 Jan 5 [cited 2019 Jan 8];2(1). Available from: http://www.imedpub.com/articles/cardiovascular-disease-and-its-determinants-public-health-issue.php?aid=18223
- 23. Freeman A, Tyrovolas S, Koyanagi A, Chatterji S, Leonardi M, Ayuso-Mateos JL, et al. The role of socio-economic status in depression: results from the COURAGE (aging survey in Europe). BMC Public Health. 2016 Oct 19;16(1):1098.
- 24. Sung MMY, Dyck JRB. Age-related cardiovascular disease and the beneficial effects of calorie restriction. Heart Fail Rev. 2012 Sep;17(4-5):707–19.
- 25. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, Age, Cardiovascular Risk Factors, and Coronary Heart Disease. Circulation [Internet]. 1999 Mar 9 [cited 2019 Feb 8]; Available from: https://www.ahajournals.org/doi/full/10.1161/01.CIR.99.9.1165
- 26. Blazer D, Burchett B, Service, Connie, George LK. The Association of Age and Depression Among the Elderly: An Epidemiologic Exploration. J Gerontol. 1991 Nov 1;46(6):M210–5.
- 27. Honjo K, Iso H, Inoue M, Tsugane S, Japan Public Health Center-based Prospective Study Group. Education, social roles, and the risk of cardiovascular disease among middle-aged Japanese women: the JPHC Study Cohort I. Stroke. 2008 Oct;39(10):2886–90.

- 28. Lee JR, Paultre F, Mosca L. The association between educational level and risk of cardiovascular disease fatality among women with cardiovascular disease. Womens Health Issues. 2005 Mar;15(2):80–8.
- 29. Bjelland I, Krokstad S, Mykletun A, Dahl AA, Tell GS, Tambs K. Does a higher educational level protect against anxiety and depression? The HUNT study. Soc Sci Med. 2008 Mar;66(6):1334–45.
- 30. Mezuk B, Eaton WW, Golden SH, Ding Y. The influence of educational attainment on depression and risk of type 2 diabetes. Am J Public Health. 2008 Aug;98(8):1480–5.
- 31. Chaturvedi N. Ethnic differences in cardiovascular disease. Heart. 2003 Jun;89(6):681–6.
- 32. Brewer LC, Cooper LA. Race, Discrimination, and Cardiovascular Disease. AMA Journal of Ethics. 2014 Jun 1;16(6):455–60.
- 33. Riolo SA, Nguyen TA, Greden JF, King CA. Prevalence of depression by race/ethnicity: findings from the National Health and Nutrition Examination Survey III. Am J Public Health. 2005 Jun;95(6):998–1000.
- 34. Maharaj RG. Depression and the nature of Trinidadian family practice: a cross-sectional study. BMC Fam Pract. 2007 Apr 26;8:25.
- 35. Kang H-J, Kim S-Y, Bae K-Y, Kim S-W, Shin I-S, Yoon J-S, et al. Comorbidity of depression with physical disorders: research and clinical implications. Chonnam Med J. 2015 Apr;51(1):8–18.
- 36. Egede LE, Nietert PJ, Zheng D. Depression and all-cause and coronary heart disease mortality among adults with and without diabetes. Diabetes Care. 2005 Jun;28(6):1339–45.
- 37. Mimura M. Comorbidity of Depression and Other Diseases. Japan Med Assoc J. 2001;44(5):225–9.
- 38. Lichtman JH, Bigger JT Jr, Blumenthal JA, Frasure-Smith N, Kaufmann PG, Lespérance F, et al. Depression and coronary heart disease: recommendations

- for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association. Circulation. 2008 Oct 21;118(17):1768–75.
- 39. Ceccarini M, Manzoni GM, Castelnuovo G. Assessing depression in cardiac patients: what measures should be considered? Depress Res Treat. 2014 Feb 6;2014:148256.
- 40. Khawaja IS, Westermeyer JJ, Gajwani P, Feinstein RE. Depression and coronary artery disease: the association, mechanisms, and therapeutic implications. Psychiatry . 2009 Jan;6(1):38–51.
- 41. Arroll B, Goodyear-Smith F, Crengle S, Gunn J, Kerse N, Fishman T, et al. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. Ann Fam Med. 2010 Jul;8(4):348–53.
- 42. Carey M, Jones KA, Yoong SL, D'Este C, Boyes AW, Paul C, et al. Comparison of a single self-assessment item with the PHQ-9 for detecting depression in general practice. Fam Pract. 2014 Aug 1;31(4):483–9.
- 43. Kohrt BA, Luitel NP, Acharya P, Jordans MJD. Detection of depression in low resource settings: validation of the Patient Health Questionnaire (PHQ-9) and cultural concepts of distress in Nepal. BMC Psychiatry. 2016 Mar 8;16:58.
- 44. Sahni A, Agius M. The Use of the PHQ9 self-rating scale to assess depression within Primary Care. Psychiatr Danub. 2017 Sep;29(Suppl 3):615–8.
- 45. Trinidad and Tobago Population 2018 (Demographics, Maps, Graphs)
 [Internet]. [cited 2019 Jan 13]. Available from:
 http://worldpopulationreview.com/countries/trinidad-and-tobago-population/
- 46. Sample Size Calculators [Internet]. [cited 2019 Jan 13]. Available from: http://hedwig.mgh.harvard.edu/sample_size/size.html

- 47. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep;16(9):606–13.
- 48. Albert PR. Why is depression more prevalent in women? J Psychiatry Neurosci. 2015 Jul;40(4):219–21.
- 49. Kuehner C. Why is depression more common among women than among men? Lancet Psychiatry. 2017 Feb;4(2):146–58.
- 50. Peyrot WJ, Lee SH, Milaneschi Y, Abdellaoui A, Byrne EM, Esko T, et al. The association between lower educational attainment and depression owing to shared genetic effects? Results in ~25,000 subjects. Mol Psychiatry. 2015 Jun;20(6):735–43.
- 51. Bauldry S. Variation in the Protective Effect of Higher Education Against Depression. Soc Ment Health. 2015 Jul;5(2):145–61.
- 52. Shi J, Zhang Y, Liu F, Li Y, Wang J, Flint J, et al. Associations of educational attainment, occupation, social class and major depressive disorder among Han Chinese women. PLoS One. 2014 Jan 31;9(1):e86674.
- 53. Sironi M. Education and mental health in Europe: School attainment as a means to fight depression. Int J Ment Health. 2012;41(3):79–105.
- 54. Patel V, Burns JK, Dhingra M, Tarver L, Kohrt BA, Lund C. Income inequality and depression: a systematic review and meta-analysis of the association and a scoping review of mechanisms. World Psychiatry. 2018 Feb;17(1):76–89.
- 55. van Deurzen I, van Ingen E, van Oorschot WJH. Income Inequality and Depression: The Role of Social Comparisons and Coping Resources. Eur Sociol Rev. 2015 Aug 1;31(4):477–89.
- 56. Martikainen P, Adda J, Ferrie JE, Davey Smith G, Marmot M. Effects of income and wealth on GHQ depression and poor self rated health in white collar women and men in the Whitehall II study. J Epidemiol Community Health. 2003 Sep;57(9):718–23.

- 57. Santos MJ dos, Kawamura HC, Kassouf AL. Socioeconomic Conditions and Risk of Mental Depression: An Empirical Analysis for Brazilian Citizens. Economics Research International [Internet]. 2012 Apr 17 [cited 2019 Feb 5];2012. Available from: https://www.hindawi.com/journals/ecri/2012/278906/
- 58. Sareen J, Afifi TO, McMillan KA, Asmundson GJG. Relationship between household income and mental disorders: findings from a population-based longitudinal study. Arch Gen Psychiatry. 2011 Apr;68(4):419–27.
- 59. Dunlop DD, Song J, Lyons JS, Manheim LM, Chang RW. Racial/ethnic differences in rates of depression among preretirement adults. Am J Public Health. 2003 Nov;93(11):1945–52.
- 60. González HM, Tarraf W, Whitfield KE, Vega WA. The epidemiology of major depression and ethnicity in the United States. J Psychiatr Res. 2010 Nov;44(15):1043–51.
- 61. Ethnic minority membership and depression in the UK and America. Mental Health and Social Inclusion [Internet]. 2017 Jan 30 [cited 2019 Feb 5]; Available from: http://www.emeraldinsight.com/doi/10.1108/MHSI-12-2016-0037
- 62. Budhwani H, Hearld KR, Chavez-Yenter D. Depression in Racial and Ethnic Minorities: the Impact of Nativity and Discrimination. J Racial Ethn Health Disparities. 2015 Mar;2(1):34–42.
- 63. Rubio-Guerra AF, Rodriguez-Lopez L, Vargas-Ayala G, Huerta-Ramirez S, Serna DC, Lozano-Nuevo JJ. Depression increases the risk for uncontrolled hypertension. Exp Clin Cardiol. 2013 Winter;18(1):10–2.
- 64. Li Z, Li Y, Chen L, Chen P, Hu Y. Prevalence of Depression in Patients With Hypertension: A Systematic Review and Meta-Analysis. Medicine . 2015 Aug;94(31):e1317.

- 65. Stage KB, Middelboe T, Stage TB, Sørensen CH. Depression in COPD-management and quality of life considerations. Int J Chron Obstruct Pulmon Dis. 2006;1(3):315–20.
- 66. Yohannes AM, Alexopoulos GS. Depression and anxiety in patients with COPD. Eur Respir Rev. 2014 Sep;23(133):345–9.
- 67. Hörnsten C, Lövheim H, Nordström P, Gustafson Y. The prevalence of stroke and depression and factors associated with depression in elderly people with and without stroke. BMC Geriatr. 2016 Oct 7;16(1):174.
- 68. Hawamdeh S, Almari AM, Almutairi AS, Dator WLT. Determinants and prevalence of depression in patients with chronic renal disease, and their caregivers. Int J Nephrol Renovasc Dis. 2017 Jul 3;10:183–9.
- 69. Shirazian S, Grant CD, Aina O, Mattana J, Khorassani F, Ricardo AC.

 Depression in Chronic Kidney Disease and End-Stage Renal Disease:

 Similarities and Differences in Diagnosis, Epidemiology, and Management.

 Kidney Int Rep. 2017 Jan;2(1):94–107.
- Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med. 2009 Sep 10;361(11):1045–57.
- 71. Yurtdas M, Ozdemir M. Ticagrelor-Associated Conduction Disorder: A Case Report and Review of the Literature. Cardiol Res Pract. 2017 Jun;8(3):123–7.
- 72. Reynolds WM. The PHQ-9 works well as a screening but not diagnostic instrument for depressive disorder. Evid Based Ment Health. 2010 Aug;13(3):96.
- 73. Padhy SK, Sarkar S, Davuluri T, Malhotra N. Depression as a risk factor for cardiac illness What do we know about? Journal of Indian College of Cardiology. 2015 Jun 1;5(2):123–30.

- 74. Ko DT, Hebert PR, Coffey CS, Sedrakyan A, Curtis JP, Krumholz HM. Beta-blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. JAMA. 2002 Jul 17;288(3):351–7.
- 75. Stanton AV. Calcium channel blockers. The jury is still out on whether they cause heart attacks and suicide. BMJ. 1998 May 16;316(7143):1471–3.
- 76. Redlich C, Berk M, Williams LJ, Sundquist J, Sundquist K, Li X. Statin use and risk of depression: a Swedish national cohort study. BMC Psychiatry. 2014 Dec 4;14:348.
- 77. Frederick FT, Maharajh HD. Prevalence of depression in type 2 diabetic patients in Trinidad and Tobago. West Indian Med J. 2013 Sep;62(7):628–31.
- 78. Mohamed R, Abdul Kadir A, Yaacob LH. A study on depression among patient with type 2 diabetes mellitus in North-Eastcoast Malaysia.
 International Journal of Collaborative Research on Internal Medicine & Public Health. 2012;4(8):1589–600.
- 79. Salinero-Fort MA, Gómez-Campelo P, San Andrés-Rebollo FJ, Cárdenas-Valladolid J, Abánades-Herranz JC, Carrillo de Santa Pau E, et al. Prevalence of depression in patients with type 2 diabetes mellitus in Spain (the DIADEMA Study): results from the MADIABETES cohort. BMJ Open. 2018 Sep 24;8(9):e020768.
- 80. Bai X, Liu Z, Li Z, Yan D. The association between insulin therapy and depression in patients with type 2 diabetes mellitus: a meta-analysis. BMJ Open. 2018 Nov 28;8(11):e020062.
- 81. Katon WJ, Lin EHB, Von Korff M, Ciechanowski P, Ludman EJ, Young B, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med. 2010 Dec 30;363(27):2611–20.
- 82. Katon W, Unützer J, Russo J. Major depression: the importance of clinical characteristics and treatment response to prognosis. Depress Anxiety. 2010;27(1):19–26.

- 83. Sinclair PA, Lyness JM, King DA, Cox C, Caine ED. Depression and self-reported functional status in older primary care patients. Am J Psychiatry. 2001 Mar;158(3):416–9.
- 84. Inoue T, Tanaka T, Nakagawa S, Nakato Y, Kameyama R, Boku S, et al. Utility and limitations of PHQ-9 in a clinic specializing in psychiatric care. BMC Psychiatry. 2012 Jul 3;12:73.
- 85. Huang FY, Chung H, Kroenke K, Delucchi KL, Spitzer RL. Using the Patient Health Questionnaire-9 to measure depression among racially and ethnically diverse primary care patients. J Gen Intern Med. 2006 Jun;21(6):547–52.
- 86. Titov N, Dear BF, McMillan D, Anderson T, Zou J, Sunderland M. Psychometric comparison of the PHQ-9 and BDI-II for measuring response during treatment of depression. Cogn Behav Ther. 2011;40(2):126–36.
- 87. van Steenbergen-Weijenburg KM, de Vroege L, Ploeger RR, Brals JW, Vloedbeld MG, Veneman TF, et al. Validation of the PHQ-9 as a screening instrument for depression in diabetes patients in specialized outpatient clinics. BMC Health Serv Res. 2010 Aug 12;10:235.